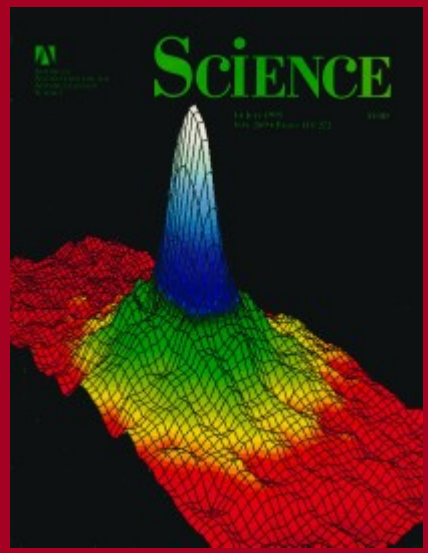
Outlining a CONSORT statement

Methods – Extension to biobank studies

Context



Epidemiology faces its limits
(Taubes, 1995)

The NEW ENGLAND JOURNAL of MEDICINE

June 22, 2000

Randomized Trials or Observational Tribulations? (Pocock & Elbourne)

A Comparison of Observational Studies and Randomized, Controlled Trials (Benson & Hartz)

Randomized, Controlled Trials, Observational Studies, and the Hierarchy of Research Designs (Concato, Shah & Horwitz)

Context

Beyond randomised versus observational studies (Concato & Horwitz)

Those confounded vitamins: what can we learn from the differences between observational versus randomised trial evidence? (Lawlor et al.)

When are observational studies as credible as randomised trials? (Vandenbroucke)

22 May, 2004

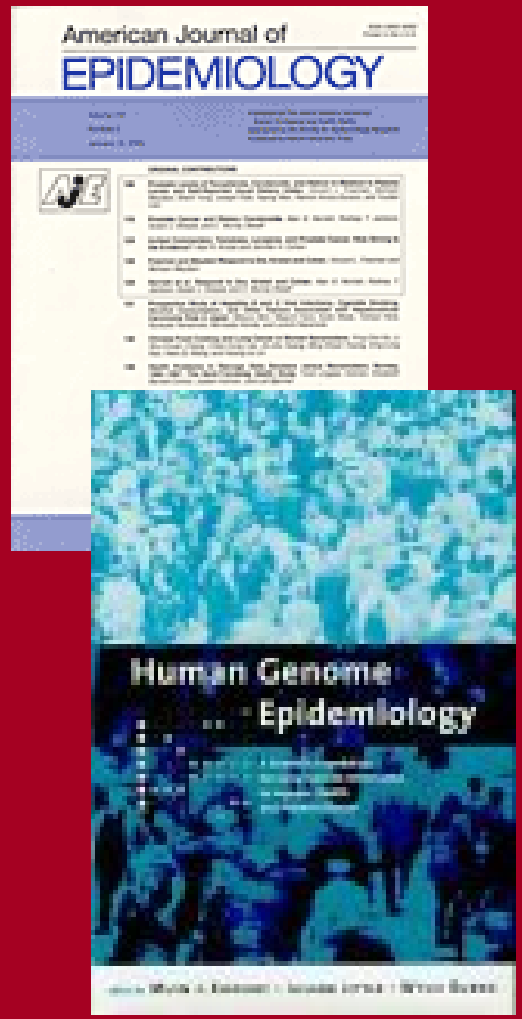
6 October, 2004

The scandal of poor epidemiological research *Reporting guidelines are needed for observational epidemiology* (von Elm & Egger)

Issues in the reporting of epidemiological studies: a survey of recent practice (Pocock et al.)

Reporting and Review of Human Genome Epidemiology Studies

- Selection of study subjects
- Analytic validity of genotyping
- Assessment of exposure
- Confounding, including population stratification
- Statistical issues



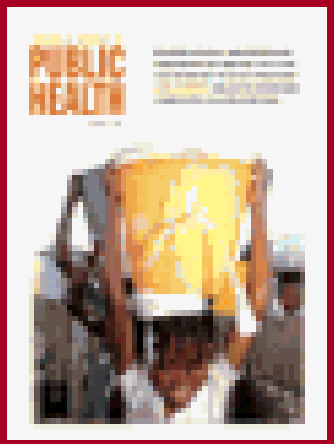
Reporting, Appraising, and Integrating Data on Genotype Prevalence and Gene-Disease Associations A*m J Epidemiol* 2002;156:300–10.

Reporting and Review of Human Genome Epidemiology Studies. In: Khoury MJ, Little J, Burke W. (Editors). *Human Genome Epidemiology: A scientific foundation for using genetic information to improve health and prevent disease.* New York, Oxford University Press, 2004, pp. 168-192.

Checklists for non-randomized evaluations of interventions

Evaluating non-randomised intervention studies
(Deeks et al., 2003)

"Although many quality assessment tools exist and have been used for appraising non-randomised studies, most omit key quality domains."



Improving the reporting quality of nonrandomized evaluations of behavioral and public health interventions: the TREND statement.
(Des Jarlais et al., 2004)

TREND: **T**ransparent **R**eporting of **E**valuations with **N**onrandomized **D**esigns

Checklists relating to cohort studies

SIGN 50:
A guideline developers' handbook
SIGN Publication No. 50, 2001
(updated 2004)
http://www.sign.ac.uk/guidelines/fulltext/50/index.html

Annex C. Critical appraisal: Notes and checklists
Methodology Checklist 3: Cohort Studies

Tooth L et al. Quality of Reporting of Observational Longitudinal Research. *Am J Epidemiol* 2005; 161: 280-8.

Draft methods checklist – single studies
(following CONSORT layout)

Participants

Initial enrolment

Eligibility criteria for participants (includes methods of recruitment)

Settings and locations where the data were collected

***Ethnic group**

***Recruitment from families** (e.g. twin pairs, index births and their parents)

**Design –* nested case-control, nested case-cohort, nested case-only

*potential issues requiring particular consideration in biobank studies

Draft methods checklist – single studies
(following CONSORT layout)

~~**Interventions**~~

Genotyping

Types of samples used†

Timing of sample collection and analysis†*

Success rate in extracting DNA†*

Definition of the genotype(s) investigated; when there are multiple alleles, those tested for should be specified

Genotyping method used (reference; for PCR methods – primer sequences*, thermocyle profile*, number of cycles*)

† Are there differences by study group, e..g. exposure status at enrolment, or in nested studies, between cases and non-cases?
*Additional information recorded (ideally in web-based methods register)

Draft methods checklist – single studies
(following CONSORT layout)

~~**Interventions**~~

Genotyping contd.

Quality control measures, including blinding of laboratory staff (to exposure; to outcome in nested studies)†*#

Samples from each group of subjects compared (e.g. cases and non-cases in nested study) included in each batch analyzed*

† Are there differences by study group, e..g. exposure status at enrolment, or in nested studies, between cases and non-cases?
* Additional information recorded (ideally in web-based methods register)
# See specific heading on blinding (masking)

Draft methods checklist – single studies
(following CONSORT layout)

~~**Interventions**~~

Exposure assessment

Methods of assessing exposures documented†

- primary exposures and confounders identified when biobank initiated
- more detailed assessments in nested studies (N.B. recall bias)

Reproducibility and validity of exposure documented

Categories or exposure scale justified

† Are there differences by study group, e..g. exposure status at enrolment, or in nested studies, between cases and non-cases?

Draft methods checklist – single studies
(following CONSORT layout)

Objectives

Specific objectives and hypotheses.

In biobank study, a major objective (and undertaking!) is establishing the biobank itself.

Some specific objectives and hypotheses formulated *a priori* (for funding agencies; depending on interests of investigators).

Others are likely to be added over time, e.g. as a result of new collaborations. These would be *a priori* hypotheses in the sense that they are not data driven, but may be secondary in the sense that the biobank was not specifically designed to test them.

Draft methods checklist – single studies
(following CONSORT layout)

Objectives contd.

Specific objectives and hypotheses

Potential combination of:

- assessment of large number of genotypes (enabled by high throughput genotyping)
- assessment of large number of exposures assessed at multiple time points
- multiple outcomes

Draft methods checklist – single studies
(following CONSORT layout)

Outcomes

Clearly defined primary and secondary outcome measures

Compared with RCT, broader range of disease outcomes likely to be assessed in a biobank study (but information about potential complications of intervention, QoL, patient-borne costs unlikely to be sought)

Scale of biobank studies means methods of outcome assessment likely to be less detailed than in RCT, e.g.

- "passive" methods of ascertainment likely to be used, e.g. linkage to cancer registration, hospital discharge data systems, vital records
- self report (positive reports verified by chart abstraction; possibly a sample of negative reports)

Draft methods checklist – single studies
(following CONSORT layout)

Outcomes contd.	*When applicable, any methods used to enhance the quality of measurements (eg,multiple observations, training of assessors).*

Draft methods checklist – single studies
(following CONSORT layout)

Sample size *How sample size was determined*

Applies to
- overall design of biobank
- nested studies

Draft methods checklist – single studies
(following CONSORT layout)

~~**Randomization**~~

Confounding

Factors associated with the outcome and exposure under investigation (that are not an intermediate step between exposure and outcome) – data collected and potential confounding assessed in analysis

Alleles associated with the outcome in linkage disequilibrium with the allele under investigation taken into account

Draft methods checklist – single studies
(following CONSORT layout)

~~**Randomization**~~

Confounding

Population stratification:

•Unaccounted variation in ethnic backgrounds by exposure group when ethnic groups tend to have different exposures and different frequencies of allelic variants

•In nested case-control study, unaccounted variation in ethnic backgrounds of cases and controls, when ethnic groups have different rates of outcome and different frequencies of allelic variants

Draft methods checklist – single studies
(following CONSORT layout)

~~**Randomization**~~

Confounding

Population stratification:

So far, empirical evidence in populations of European origin suggests magnitude of any bias small (Wacholder et al., 2000; Ardlie et al., 2002; Freedman et al., 2004; Khlat et al., 2004; Wang et al., 2004)

Interpretation of empirical evidence for African American populations mixed (Millikan et al., 2001; Ardlie et al., 2002; Freedman et al., 2004)

Likely to be less of a problem for cohort studies and studies nested within them than for case-control studies.

Draft methods checklist – single studies
(following CONSORT layout)

Blinding (masking)	Whether or not those assessing the outcomes were blinded to exposure status and genotype. Whether or not those assessing the genotypes • blinded to exposure status • in nested study, blinded to outcome

Draft methods checklist – single studies
(following CONSORT layout)

Statistical methods

Distinguish clearly *a priori* hypotheses and hypotheses generated

Statistical methods used to
- Assess associations
- Test for gene-exposure interaction

Methods to take account of
- loss to follow-up
- potential confounding
- missing data

Methods (& justification) for additional analyses, such as subgroup analyses